Remarks

Applicant requests reconsideration on the merits of the above-referenced patent application.

I. Amendments to the Specification

The amendments to the specification are shown on pages 2-7 above. Applicant submits that none of the amendments add new matter. More specifically:

Paragraph 26 has been amended to correspond to Paragraph 26 as originally filed. This amendment corrects an obvious error made in Applicant's December 6, 2001 Preliminary Amendment B, which unintentionally replaced original Paragraph 26 with an amended version of Paragraph 25.

Other amendments simply rephrase the specification, or correct grammatical or obvious errors. Applicant submits that such amendments are permissible under MPEP §2163.07.

II. Claim Amendments

This amendment cancels claims 117 and 118, and adds new claims 139-145. Thus, claims 85, 87-92, 94-97, 99-102, 105-108, 110-113, 116, 119, 121-126, 128, 129, 131-136, and 138-145 are pending. Claims 85, 95, 106, 119, and 129 have been amended. All the claims, including the amendments, are shown on pages 8-14 above. Applicants submit that the amendments and new claims do not introduce any new matter. Specifically:

The C_{max} range recited in new claims 139 and 143 is supported by Applicant's specification at, for example, the observed C_{max} results in Table 3 in Example XII on page 36. Specifically, the "2.2" value is obtained as follows:

$$2.2 = \frac{612.6 - 187.1}{158.5 + 31.0}$$

The t_{max} range recited in new claims 140, 141, 144, and 145 is supported by Applicant's specification at, for example, the observed t_{max} results in Table 3 in Example XII on page 36. Specifically, the "38%" value is obtained as follows:

$$38\% = \frac{0.63 + 0.23}{2.75 - 0.46} \times 100\%$$

New claim 142 recites a method wherein the substance is a low molecular weight heparain. It characterizes the heparin as being dalteparin, which is the generic name for Fibrin. Claim 143 is supported by Applicant's specification at, for example, Ex. VIII-XI on pages 33-35.

Other amendments simply rephrase the claims. Applicants submit that such amendments are permissible under MPEP §2163.07.

Applicants reserve the right to pursue any previously canceled subject matter and/or any other subject matter disclosed in this application in one or more later-filed divisional and/or continuation applications.

III. Response to the rejection of claims 85, 87, 90, 91, 94-97, 99, 105-108, 110, 116, 119, 121, 124, 125, 128, 129, 131, 134, 135, and 138 under 35 U.S.C. §102(b)

Claims 85, 87, 90, 91, 94-97, 99, 105-108, 110, 116, 119, 121, 124, 125, 128, 129, 131, 134, 135, and 138 have been rejected under 35 U.S.C. §102(b) as lacking novelty over Gross et al. (U.S. Patent No. 5,848,991). Applicant respectfully requests withdrawal of this rejection. Applicant submits that Gross et al. fail to disclose, either expressly or inherently, each and every element of any of the rejected claims.

Independent claims 85, 95, 106, 119, and 129 all recite injecting a substance into the dermis via "bolus administration". Gross et al. fail to disclose injection by bolus administration. Instead, Gross et al. repeatedly discuss use of their device for administering a drug at a **slow** rate. For example, Gross et al. state that the device "allows the drug to be delivered at precisely controllable **slow** rates." *See, e.g.*, col. 4, lines 29-35 (emphasis added). *See also* Abstract, lines 13-15; col. 2, lines 22-25; and col. 7, lines 47-49. Because Gross et

al. fail to disclose bolus administration, claims 85, 95, 106, 119, and 129 must be found to be novel over Gross et al.

All the remaining rejected claims depend directly or indirectly from claim 85, 95, 106, 119, or 129, and are therefore novel over Gross et al. for at least the same reasons as claim 85, 95, 106, 119, or 129.

IV. Response to rejection of claims 85, 87-91, 94-97, 99, 100, 101, 105-108, 110, 111, 112, 116, 119, 121-125, 128, 129, 131-135, and 138 under 35 U.S.C. §103(a)

Claims 85, 87-91, 94-97, 99, 100, 101, 105-108, 110, 111, 112, 116, 119, 121-125, 128, 129, 131-135, and 138 have been rejected under 35 U.S.C. §103(a) for being obvious over Gross et al. in view of D'Antonio et al. (U.S. Patent No. 6,056,716) or in view of Puri et al. (*An Investigation of the Intradermal Route as an Effective Means of Immunization for Microparticulate Vaccine Delivery Systems*, Vaccine 18 (2000) 2600-12). Applicant respectfully requests withdrawal of this rejection.

As noted above, independent claims 85, 95, 106, 119, and 129 all recite injecting a substance into the dermis via "bolus administration". Gross et al. fail to teach, suggest, or provide motivation for bolus administration. Thus, claims 85, 95, 106, 119, and 129 cannot be *prima facie* obvious in view of Gross et al. alone. *See* MPEP §2143 ("[t]o establish a *prima facie* case of obviousness, . . . the prior art reference . . . must teach or suggest all the claim limitations."). In fact, Gross et al. teach away from Applicant's claims by repeatedly emphasizing the use of their device for administering a drug at a slow rate:

> The device permits devivery of drugs . . . at **slow rates** . . . . Abstract, lines 13-15 (emphasis added).
>
> As will be described more particularly below, such an intradermal drug delivery device permits the delivery of a variety of drugs . . . at **slow rates** . . . . Col. 2, lines 22-25 (emphasis added).
>
> Such an intradermal delivery device . . . allows the drug to be delivered at precisely controllable **slow rates**. Col. 4, lines 29-35 (emphasis added).
>
> These dimensions permit a **slow, precisely-controllable delivery of the drug** . . . . Col. 7, lines 47-49 (emphasis added).

This teaching away further evidences a lack of *prima facie* obviousness in view of Gross et al. alone. *See* MPEP §2145 ("A prior art reference that 'teaches away' from the claimed invention is a significant factor to be considered in determining obviousness.").

The discussions in D'Antonio et al. and Puri et al. fail to address the shortcomings of Gross et al.'s discussion. Claims 85, 95, 106, 119, and 129 recite "a low molecular weight heparin" or "a dopamine receptor agonist." The Office action states that D'Antonio et al. and Puri et al. disclose that medication delivered intradermally results in improved systemic absorption, and that it would therefore have been obvious to a skilled artisan to modify the method of Gross et al. with the teachings of D'Antonio et al. or Puri et al. At the outset, both references fail to teach, suggest, or provide motivation for administering a heparin or dopamine receptor agonist. To the contrary, the discussions in both references relating to absorption via intradermal injection are specific to the field of immunology. In particular, D'Antonio et al. state that "both veterinary and human **immunologists** have cited experimental evidence indicating that injections into the dermis may be many times more potent than that of the IM or subcutaneous regions". Col. 29, lines 3-9 (emphasis added). And Puri et al. discuss better absorption of microparticulate **vaccines** through intradermal, rather than subcutaneous, administration. *See, e.g.,* Abstract, p. 2601, pp. 2607-10. Puri et al. speculate that intradermal injection of vaccines may be more effective than subcutaneous injection because intradermal administration positions the vaccine near immune-competent cells in the epidermal and dermal layers of the skin. *See* pp. 2608-09. Such reasoning would not have provided any motivation for a skilled artisan to use intradermal bolus administration for a low molecular weight heparin or dopamine receptor agonist.

Simply put, Gross et al., whether viewed alone or in combination with the other cited references, fail to support a *prima facie* case of obviousness for bolus intradermal administration of a low molecular weight heparin or dopamine receptor agonist. If anything, a skilled artisan reading these references would have been steered away from bolus administration and toward administering a drug at a slow rate due to the repeated instruction in Gross et al. for delivering substances at such a rate. Thus, claims 85, 95, 106, 119, and 129 are patentable over the cited references.

All the remaining rejected claims depend directly or indirectly from claim 85, 95, 106, 119, or 129, and are therefore patentable over the cited references for at least the same reasons as claim 85, 95, 106, 119, or 129.

V. Response to the rejection of claims 92, 102, 113, 126, and 136 under 35 U.S.C. §103(a)

Claims 92, 102, 113, 126, and 136 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Gross et al. in view of D'Antonio et al. or Puri et al., and further in view of Ganderton et al. (U.S. Patent No. 3,814,097). Applicant respectfully requests withdrawal of this rejection.

This rejection relies on the previous rejection of claims 91, 97, 107, 125, and 135 as being unpatentable over Gross et al. in view of D'Antonio et al. or Puri et al. As discussed above, Gross et al., even when combined with D'Antonio et al. or Puri et al., fail to support a *prima facie* case of obviousness as to these claims. Claims 92, 102, 113, 126, and 136 are therefore necessarily patentable over these three references as well. This conclusion does not change even if these references are viewed in combination with Ganderton et al. Specifically, Ganderton et al. fail to even remotely disclose that bolus intradermal administration of a low molecular weight heparin or a dopamine receptor agonist resulting in improved systemic absorption relative to subcutaneous injection. Thus, all four references, even when combined, fail to support a *prima facie* case of obviousness as to claim 92, 102, 113, 126, and 136. If anything, a skilled artisan reading these references would have been steered away from bolus administration and toward administering a drug at a slow rate due to the repeated instruction in Gross et al. for delivering substances at such a rate. Thus, claims 92, 102, 113, 126, and 136 are patentable over all four cited references.

* * * * * * * * *

Applicant hereby requests a two-month extension for responding to the May 9, 2005 Office action, and have enclosed a check to cover that extension. Applicant believes that no additional fee is due in connection with this filing. If, however, Applicant does owe any such fee(s), the Commissioner is hereby authorized to charge the fee(s) to Deposit Account No. **08-**

0750. In addition, if there is ever any other fee deficiency or overpayment under 37 C.F.R. §1.16 or 1.17 in connection with this patent application, the Commissioner is hereby authorized to charge such deficiency or overpayment to Deposit Account No. **08-0750**.

Applicant submits that the pending claims are in condition for allowance, and requests that this application be allowed.

Respectfully submitted,

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CERTIFICATE OF MAILING UNDER 37 CFR § 1.8

I certify that this correspondence is being deposited with the U.S. Postal Service on **September 22, 2005** with sufficient postage as first class mail (including Express Mail per MPEP §512), and addressed to **Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450**.

DMG/CLR/PML